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Hypotension Associated With Nesiritide Infusion in Patients With Decompensated Heart Failure Is Related to Large Volume Diuresis: Implications for Monitoring and Dose Adjustments

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Background: Predictors and clinical course of hypotension following nesiritide infusion in patients with decompensated heart failure have not been established.

Methods: We established a prospective registry of consecutive patients with decompensated heart failure treated with nesiritide at the Cleveland Clinic, with standardized monitoring and titration procedures. Patients with suspected low filling pressures, cardiogenic shock, or systolic blood pressure <90mmHg were restricted from receiving nesiritide therapy by drug utilization guidelines. Hypotension was defined as systolic blood pressure <80 mmHg for 2 or more measurements.

Results: A total of 92 consecutive patients initiated on nesiritide infusions were evaluated (mean age 64 ±13 years, 60% male, 64% Caucasians, mean LVEF 29 ±16%, mean plasma BNP 964 ±367 pg/mL). Within 24 hours of nesiritide infusion, asymptomatic and symptomatic hypotension occurred in 26% and 8% of patients respectively. One patient experienced symptomatic hypotension leading to myocardial infarction. Patients experiencing hypotension were more likely to have prolonged infusion >48 hours (72% vs 48%, p<0.05), and less dose adjustments of diuretics and nesiritide (67% vs 21%, p<0.05) than non-hypotensive patients. The majority (79%) of hypotensive patients did not experience any episodes of low blood pressure until after >12 hours of nesiritide infusion. In addition, large volume diuresis (net loss >2 liters over 24 hours) was associated with more hypotension than lower volume diuresis (36% versus 20%, p=0.03), even when adjusted for baseline systolic blood pressure and disease severity (such as LV function, baseline NYHA class) in multivariable analysis.

Conclusions: Hypotension associated with nesiritide infusion in patients with decompensated heart failure occurs, and seems to more often accompany large volume diuresis. Although nesiritide infusion was well tolerated in the majority of patients, urinary output (particularly in later phase of infusion) should be closely monitored. Urine output response to nesiritide should be used to guide dose adjustments of diuretics/nesiritide.

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Hemodynamic Effects of Intravenous Nesiritide in Patients With Pulmonary Hypertension

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Background: Nesiritide (Natrecor®, Scios Inc, Fremont, CA) is a recombinant human B-type natriuretic peptide, that has been shown to be beneficial in patients with decompensated heart failure. This study evaluated the effects of intravenous nesiritide on right heart hemodynamics in patients with pulmonary hypertension (PH).

Methods: Patients referred for right cardiac catheterization with a mean pulmonary artery (PA) pressure >25mmHg and a right atrial (RA) pressure >7mmHg were enrolled. Patients who had baseline SBP ≤95 mmHg, were on vasopressors, or had received diuretics, nitroglycerin, or calcium blockers within the previous 12 hours were excluded. Right heart catheterization was performed at baseline and 15- and 30-minutes after an IV nesiritide infusion (2mcg/kg bolus and 0.01mcg/kg/min).

Results: Twelve patients were enrolled to date, with a goal of 20 patients. Seven patients had postcapillary PH (PCW >15mmHg), while 5 had precapillary PH (PCW ≤15mmHg). For patients with postcapillary PH, the mean age was 59±15 years, all were male, and 3 had ischemic cardiomyopathy. Mean LVEF was 27±18%. At baseline, mean RA pressure was 10±1mmHg, mean PA pressure was 42±7mmHg, and PCW pressure was 25±7mmHg. After the 30-min nesiritide infusion, RA pressure decreased 52% (p=0.006), mean PA pressure decreased 31% (p=0.0007), PCW pressure decreased 46% (p=0.002), pulmonary vascular resistance (PVR) decreased 35% (p=0.03), arteriovenous oxygen difference (AVDO2) decreased 26% (p=0.002), and cardiac output (CO) increased 33% (p=0.03). For patients with precapillary PH, the mean age was 59±12 years, 60% were female, and 60% had PPH. Mean LVEF was 63±6%. At baseline, mean RA pressure was 13±6mmHg, mean PA pressure was 43±6mmHg, and PCW pressure was 10±4mmHg. While the mean aortic pressure decreased 9% (p=0.04), there was no change in RA, PA, or PCW pressure, nor any change in CO, PVR, or AVDO2.

Conclusion: Nesiritide significantly reduces PA pressure, PVR, and biventricular filling pressures in patients with postcapillary PH at 15- and 30-minutes. In this small cohort of patients with precapillary PH studied so far, nesiritide has no significant acute hemodynamic effect on the pulmonary vasculature.

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Does Improvement of Left Ventricular Ejection Fraction in Patients With Viable Myocardium Persist Over the Long-Term After Coronary Revascularization?

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Background: In patients with ischemic cardiomyopathy, left ventricular ejection fraction (LVEF) after coronary revascularization is likely to improve if a substantial amount of viable myocardium is present. The aim of this study was to evaluate whether this improvement in LVEF is sustained at long-term follow-up.

Methods: Viability was assessed by dobutamine stress echocardiography (DSE) in 63 patients with ischemic cardiomyopathy (LVEF 31±8%); patients were already scheduled for revascularization. LVEF was assessed by radionuclide ventriculography before, 1 and 4 years after revascularization. An improvement of LVEF ≥ 5% after revascularization was considered clinically significant.

Results: According to DSE, 256/593 (43%) severely dysfunctional segments were viable

and 337 (57%) were scarred. A substantial amount of viable myocardium (≥ 4 segments) was present in 31 patients (viable patients). Clinical characteristics were comparable between patients with and without a substantial amount of viable myocardium. One year after revascularization, LVEF improved ≥ 5% in 22 viable patients (71%, P<0.001 vs non-viable) and remained improved at 4 years follow-up in 21 (95%) of them. Although, LVEF did not improve at one year in 9 viable patients, 3 of them (33%) exhibited late recovery at 4 years follow-up. In 91% of the non-viable patients, LVEF did not improve at one nor at 4 years follow-up.

Conclusion: Patients with ischemic cardiomyopathy and a substantial amount of viable myocardium have a high likelihood to improve in LVEF after coronary revascularization; this improvement in LVEF is sustained at 4 years follow-up. Interestingly, even after one year post-revascularization, some patients still exhibit additional improvement in LVEF.

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External Counterpulsation Improves Cardiac Outcomes in Patients With Chronic Heart Failure

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Background: ECP is a noninvasive treatment modality in patients with intractable chronic angina. They are designed to decrease cardiac workload while increasing myocardial perfusion pressure. There is a theoretical possibility that by compressing the venous beds in the legs, an ensuing increase in preload could potentially worsen pulmonary congestion in patients with CHF. However, by careful setting of cuff pressures, there is a potential to improve angiogenesis, nitric oxide production and myocardial perfusion thus enhancing left ventricular performance. This study sought to analyze outcomes in CHF with ECP therapy.

Methods: Data from a consecutive 130 patients from the ECP patient registry was evaluated with one year follow up. Patients were in NYHA Class I-IV CHF and Canadian classification for angina Class III or IV. All patients were serially treated with CardiAssist™ ECP system (Cardiomedics Inc., Irvine, CA). All patients received 35 treatments (one hour per day, 5 days a week for 7 weeks). Baseline one year follow up data were compared on demographics, NYHA and angina class, ejection fraction, hospitalization, and mortality.

Results: Of 130 patients (80% male) with mean age 67.2 +/- and mean EF 0.33 +/- 0.18, there were 23% in NYHA Class I, 21.5% in Class II, 62% in III and 18% in Class IV. Hospitalization was reduced from 1.8 admissions to 0.5 over a 12 month period (72% reduction p<.001 in all NYHA Classes). LVEF improved from 0.33 to .41 (p<.001). NYHA Class improved from 2.85 to 2.03 (28% improvement, p<.001). Class III patients improved by 1.5 class and NYHA Class IV improved by 2 classes. Seven out of 130 (5.4%) patients died, of which 6 were Class IV patients. There were no adverse events or withdrawals.

Conclusion: ECP is a safe and effective treatment for CHF in patients with angina. ECP improves functional class and ejection fraction, reduces hospitalization and reduces mortality.

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Effects of Acupuncture Compared With Placebo-Acupuncture on Autonomic Function, Exercise Tolerance, and Quality of Life in Patients With Heart Failure: A Randomized Controlled Single-Blind Pilot Study

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Background: Heart failure is characterized by autonomic dysfunction. This pilot study investigated effects of acupuncture on autonomic function, exercise tolerance (ET) and quality of life (QoL) in patients with heart failure. **Methods:** 17 patients with stable NYHA class II or III (left ventricular ejection fraction 30±10%, peak oxygen uptake 15.2±1.2 ml/min/kg, six minute walk distance 438±31 m) were randomized to receive acupuncture (n=9) or noninvasive placebo-acupuncture (n=8) at 13 acupoints in 10 sessions. 30 min after the first and last session the parasympathetic and sympathetic response to orthostatic stress (tilt-table) were analyzed by the high-frequency power spectral component (HF) and norepinephrine plasma levels (NE). Before and 4 weeks after treatment ET and QoL were assessed by 6 minute walk test, SF36 and the Minnesota Living with Heart Failure Score. **Results:** At the first session acupuncture abolished the orthostatic stress induced withdrawal of HF (-4%) compared with placebo (-30%, p=0.038). Simultaneously, NE increased in the acupuncture group (+42%, p=0.007) but not significantly in the placebo group (+18%), indicating an intact sympathetic response to prevent vasodilation caused by the missing parasympathetic withdrawal. Likewise, no decrease in arterial blood pressure occurred. At the last session acupuncture exerted the same effects on HF and NE but placebo did also, suggesting that the placebo needle induces conditioning of acupoints by acupressure-like effects. Four weeks after the last session the six minute walk distance was improved in the acupuncture group by 27±8 m (p=0.009) but not in the placebo group (-1±11 m). Slight but not significant improvements in QoL were observed in both the acupuncture and placebo group. Furthermore, no bleeding complications at acupoints in the anticoagulated patients occurred. **Conclusion:** Acupuncture in patients with heart failure at 13 in this study used acupoints (I) prevents stress induced parasympathetic withdrawal but does not inhibit systemic sympathetic response and (II) improves exercise tolerance. (III) Further studies are warranted to confirm the results of this pilot study in a larger heart failure population.